

**WHAT IS CLAIMED IS:**

1. A method for increasing the susceptibility of epithelial cells to viral infection comprising increasing the transepithelial permeability of epithelial tissue comprising said cells.
2. The method of claim 1, wherein said epithelial tissue is airway epithelial tissue.
3. The method of claim 2, wherein said airway epithelial tissue is bronchial tissue.
4. The method of claim 2, wherein said airway epithelial tissue is tracheal tissue.
5. The method of claim 2, wherein said airway epithelial tissue is alveolar tissue.
6. The method of claim 1, further comprising increasing the proliferation of said epithelial cells.
7. The method of claim 6, wherein increasing the proliferation of said epithelial cells is achieved by contacting said cells with a proliferative factor.
8. The method of claim 7, wherein said proliferative factor is a growth factor.
9. The method of claim 1, wherein increasing the intraepithelial permeability of said epithelial tissue is achieved by ~~contacting~~ cells of said epithelial tissue with a tissue permeabilizing agent.
10. The method of claim 9, wherein said tissue permeabilizing agent is a hypotonic solution.
11. The method of claim 9, wherein said tissue permeabilizing agent is ion chelator.

12. The method of claim 11, wherein said ion chelator is EGTA, BAPTA or EDTA.
13. The method of claim 9, wherein said tissue permeabilizing agent is a cationic peptide.
- 5 14. The method of claim 13, wherein said cationic peptide is poly-L-lysine.
15. The method of claim 9, wherein said tissue permeabilizing agent is an occludin peptide.
- 10 16. The method of claim 9, wherein said tissue permeabilizing agent is a cytoskeletal disruption agent.
- 15 17. The method of claim 16, wherein said cytoskeletal disruption agent is cytochalasin B or colchicine.
18. The method of claim 9, wherein said tissue permeabilizing agent is ether or glycerol.
- 20 19. The method of claim 9, wherein said tissue permeabilizing agent is a neurotransmitter.
20. The method of claim 19, wherein said neurotransmitter is capsianoside.
- 25 21. The method of claim 9, wherein said tissue permeabilizing agent is FCCP.
22. The method of claim 9, wherein said tissue permeabilizing agent is an oxidant.
23. The method of claim 22, wherein said oxidant is hydrogen peroxide or ozone.
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24. The method of claim 9, wherein said tissue permeabilizing agent is a mediator of inflammation.

25. The method of claim 24, wherein said mediator of inflammation is  $\text{TNF}\alpha$ .

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26. The method of claim 1, further comprising infecting said epithelial tissue with a virus vector selected from the group consisting of a retrovirus, a lentivirus, an adenovirus, an adeno-associated virus, a parvovirus, a papovavirus, paramyxovirus and a vaccinia virus.

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27. The method of claim 26, wherein the virus vector comprises a non-viral gene under the control of a promoter active in eukaryotic cells.

28. The method of claim 27, wherein said non-viral gene is a human gene.

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29. The method of claim 28, wherein said gene encodes a polypeptide selected from the group consisting of a tumor suppressor, a cytokine, an enzyme, a toxin, a growth factor, a membrane channel, an inducer of apoptosis, a transcription factor, a hormone and a single chain antibody.

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30. The method of claim 26, wherein the virus vector is a replication-defective virus.

31. The method of claim 30, wherein the virus vector is a retroviral vector.

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32. The method of claim 1, wherein said epithelial tissue is diseased.

33. The method of claim 32, wherein said disease is lung cancer, tracheal cancer, asthma, surfactant protein B deficiency, alpha-1-antitrypsin deficiency or cystic fibrosis.

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34. The method of claim 7, wherein said proliferative factor is delivered as an aerosol.

35. The method of claim 7, wherein said proliferative factor is delivered as a topical solution.

5 36. The method of claim 9, wherein said tissue permeabilizing agent is delivered as an aerosol.

37. The method of claim 9, wherein said tissue permeabilizing agent is delivered as a topical solution.

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~~38.~~ A composition suitable for aerosol application comprising a tissue permeabilizing agent and a cell proliferative factor.

15 39. The composition of claim 38, wherein said tissue permeabilizing agent is a hypotonic solution, a cytokine, a cationic peptide, a cytoskeletal disruptor, a mediator of inflammation, an oxidant, a neurotransmitter or an ion chelator.

40. The composition of claim ~~38~~, further comprising a packaged viral vector.

20 41. The composition of claim 40, wherein said packaged viral vector comprises a non-viral gene.

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~~13~~  
42. The composition of claim 40, wherein said packaged viral vector is a retroviral vector.

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~~43.~~ A composition suitable for topical application comprising a tissue permeabilizing agent and a cell proliferative factor.

30 44. The composition of claim 43, wherein said tissue permeabilizing agent is a hypotonic solution, a cytokine, a cationic peptide, a cytoskeletal disruptor, a mediator of inflammation, an oxidant, a neurotransmitter or an ion chelator.

45. The composition of claim 43, further comprising a packaged viral vector.

46. The composition of claim 45, wherein said packaged viral vector comprises a  
5 non-viral gene.

47. The composition of claim 45, wherein said packaged viral vector is a retroviral  
vector.

10 48. A method for redistributing viral receptors on epithelial cells of an epithelial  
tissue comprising increasing the transepithelial permeability of said epithelial tissue.

49. The method of claim 48, wherein said receptor is a retroviral receptor.

15 50. A method for expressing a polypeptide in cells of an epithelial tissue comprising:

- 20 (a) providing a packaged viral vector comprising a polynucleotide  
encoding said polypeptide;  
(b) increasing the permeability of said epithelial tissue; and  
(c) contacting cells of said epithelial tissue with said packaged viral vector  
under conditions permitting the uptake of said packaged viral vector by  
said cells and expression of said polypeptide therein.

25 51. The method of claim 50, further comprising increasing the proliferation of cells of  
said epithelial tissue.

52. The method of claim 50, wherein said viral vector is a retroviral vector.

30 53. A method for treating an epithelial tissue disease comprising:

- (a) providing a packaged viral vector comprising a polynucleotide encoding said therapeutic polypeptide;
- (b) increasing the permeability of the diseased epithelial tissue; and
- (c) contacting cells of said epithelial tissue with said packaged viral vector under conditions permitting the uptake of said packaged viral vector by said cells and expression of said therapeutic polypeptide therein,
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- whereby expression of said therapeutic polypeptide treats said disease.

54. The method of claim 53, further comprising increasing the proliferation of cells of said diseased epithelial tissue.

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55. The method of claim 53, wherein the diseased epithelial tissue is airway tissue.

56. The method of claim 55, wherein said diseased airway tissue is alveolar tissue, bronchial tissue or tracheal tissue.

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57. The method of claim 53, wherein said disease is a cancer.

58. The method of claim 57, wherein said cancer is lung cancer.

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59. The method of claim 57, wherein said cancer is tracheal cancer.

60. The method of claim 53, wherein said disease is an inherited genetic defect.

61. The method of claim 60, wherein said inherited genetic defect is surfactant protein B deficiency.

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62. The method of claim 60, wherein said inherited genetic defect is alpha-1-antitrypsin deficiency.

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63. The method of claim 60, wherein said inherited genetic defect is cystic fibrosis.

64. The method of claim 53, wherein said therapeutic polypeptide is selected from the group consisting of a tumor suppressor, a cytokine, an enzyme, a toxin, a growth factor, a membrane channel, an inducer of apoptosis, a transcription factor, a hormone and a single chain antibody.

65. The method of claim 53, wherein increasing the permeability of the diseased epithelial tissue comprises contacting cells of said diseased epithelial tissue with a tissue permeabilizing agent.

66. The method of claim 54, wherein increasing the proliferation of cells of said diseased epithelial tissue comprises contacting said cells with a proliferative agent.

67. The method of claim 53, wherein said viral vector is a retroviral vector.

68. A composition comprising EGTA and in a hypotonic solution.

69. The composition of claim 68, further comprising a packaged viral vector.

70. A method for increasing the susceptibility of epithelial cells to viral infection comprising delivering to said epithelial cells a packaged viral vector and EGTA in a hypotonic solution.